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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/155,739	09/11/1998	MARY M. BENDIG	15270-001430	9068

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Teresa Stanek Rea, ESQ
Burns Doane Swecker & Mathis, LLP
1737 King Street, Suite 500
Alexandria, VA 22314

EXAMINER	
GAMBEL, PHILLIP	
ART UNIT	PAPER NUMBER
1644	22

DATE MAILED: 01/13/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/155739	BENDIG	
	Examiner	Art Unit	
	GAMBEL	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☑ Responsive to communication(s) filed on 10/24/01

2a)☑ This action is FINAL. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☑ Claim(s) ___ is/are pending in the application. 1 and 18-27

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☑ Claim(s) _____ is/are rejected. 1 and 18-27

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on ___ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☑ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☐ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____.
4)☐ Interview Summary (PTO-413) Paper No(s). ____.
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other:

DETAILED ACTION

1. Applicant's amendment, filed 10/24/02 (Paper No. 19), has been entered.
Claims 2-17 have been canceled.
Claims 1, 18 and 19 have been amended.
Claim 27 has been added.

Claims 1 and 18-27 as it reads on the election of rheumatoid arthritis are under consideration in the instant application.

Claims 2-16 have been withdrawn from further consideration by the examiner, 37 C.F.R. § 1.142(b) as being drawn to a nonelected species.

2. The text of those sections of Title 35 USC not included in this Action can be found in a prior Action.
This Office Action will be in response to applicant's arguments, filed 10/24/02 (Paper No. 19).
The rejections of record can be found in the previous Office Action (Paper No. 15).

3. Again, it is noted that a number of pages in the specifications have faint or missing words.

Applicant may consider providing a substitute specification or may consider discussing the issue with the examiner in order to correct the deficiencies in the specification.

If a substitute specification is submitted to correct the numerous entries to be amended in the specification, then the substitute specification filed must be accompanied by a statement that it contains no new matter. Such statement must be a verified statement if made by a person not registered to practice before the Office.

4. Applicant's amendment of the first line of the specification to indicate priority is acknowledged.

Applicant submits that the instant claims the benefit of, at least, the 11/21/95 priority filing date, which is the filing date of USSN 08/561,521, now U.S. Patent No. 5,840,299. Applicant relies upon the disclosure therein of methods of using the 21.6 monoclonal antibody to block α4-dependent interactions of the VLA-4 receptor, including the treating of rheumatoid arthritis.

However, USSN 08/561,521, now U.S. Patent No. 5,840,299 does not appear to provide sufficient written support for the disclosure of methods of using the humanized 21.6 antibody for "manufacturing a medicament for treating rheumatoid arthritis".

Applicant has not provided sufficient documentary support for the written description of "manufacturing a medicament for treating rheumatoid arthritis" in USSN 08/561,521, now U.S. Patent No. 5,840,299.

It is noted that entitlement to a filing date does not extend to subject matter which is not disclosed, but would be obvious over what is expressly disclosed. Lockwood v. American Airlines Inc., 41 USPQ2d 1961 (Fed. Cir. 1977).

Therefore, the filing date of the instant claims is deemed to be the filing date of the priority application PCT US96/18807, filed 11/21/96, as the earlier priority applications do not provide written support for "manufacturing a medicament for treating rheumatoid arthritis" (as well as the other non-elected diseases), and thus does not support the claimed limitations of the instant application.

5. Formal drawings, filed 10/24/02 (Paper No. 21) comply with 37 CFR 1.84.

6. Applicant's arguments with respect to the previous rejection of claim 17 under 35 U.S.C. § 112, first paragraph, are acknowledged. However, applicant's arguments are rendered moot given the cancellation of claim 17.

With respect to the assertions that a deposit is not required because the biological materials are known and publicly available, the following is noted.

Biological materials must be known and readily available to the public (See MPEP 2404.01). Neither concept alone is sufficient. The fact that applicant and other members of the public were able to obtain the materials in question from a given depository prior to and after the filing date of the application does not establish the upon issuance of a patent on the application that such material would continue to be accessible to the public. The applicant did not make of record any of the facts and circumstances surrounding the access to the biological materials from the depository, nor is there any evidence as to the depository's policy regarding the material if a patent would be granted. Further, there is no assurance that the depository would allow unlimited access to the material if the application has matured into a patent. In the absence of evidence that the 21.6 antibody / hybridoma is readily available to the public and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be irrevocably removed upon the granting of a patent.

Again, it is noted that the sequence of an entire immunoglobulin satisfies the biological deposit of said immunoglobulin. Note that satisfaction for the biological deposit of the specific 21-6 antibody requires the disclosure and recitation of its entire amino acid sequence and not based upon partial sequences

Applicant's arguments would not have been found persuasive and the rejection would have been maintained.

7. Applicant's amended claim 1, filed 10/24/02 (Paper No. 19), has obviated the previous rejection under 35 U.S.C. § 102(e) as being anticipated by Wayner et al. (U.S. Patent No. 5,730,978).

8. Claims 1 and 18-27 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Wayner et al. (U.S. Patent No. 5,730,978) in view of Bendig et al. (WO 95/19790;IDS, #10) essentially for the reasons of record set forth in Paper No. 15.

Applicant's arguments, filed 10/24/02 (Paper No. 19), have been fully considered but are not found convincing essentially for the reasons of record.

Applicant traverses this rejection for the reasons previously set forth in the Amendment and Reply dated 10/17/01; however, it is unclear what communication is being relied upon, given that no paper in this file application is dated 10/17/01.

Applicant's comments on the criteria of obviousness are acknowledged.

Applicant asserts that the prior art fails to teach or suggest the treatment of rheumatoid arthritis as well as the use of the particular humanized 21.6 antibody to treat rheumatoid arthritis.

Applicant's comments, including the reliance upon Bergsteinsdottier et al. (J. Immunol. 164: 1564-1568, 2000), Kuby et al. (Immunology, Chapter 20: Autoimmunity, pages 477-492, W.H. Freeman and Co. 1998) and Corthay et al. (International Immunology 11: 1065-1073, 1999) concerning the divergent etiologies and symptoms of multiple sclerosis and rheumatoid arthritis are acknowledged.

It should be noted that these references mainly address the differences in the genetic underpinnings of the multiple sclerosis and rheumatoid arthritis as well as the role of γδ T cells and not the commonality of targeting α4 to inhibit the inflammatory response associated with both diseases, taught by the prior art and disclosed in the instant specification as well.

Further, it is noted that it was known in the art that pathogenic and protective roles have been ascribed to Th1 cells in inflammatory autoimmune diseases such as multiple sclerosis, diabetes and rheumatoid arthritis, as evidenced by Lafaille et al. (J. Exp. Med. 186: 307-312, 1997) (see Introduction). It is acknowledged that EAE is a demyelinating disease of the central nervous system widely used as an animal model for multiple sclerosis. Experimental models of autoimmune diseases can rely upon the induction by immunization with specific tissues, such that basic myelin protein is employed for EAE and collagen is employed for arthritis, as evidenced by van Bekkum (J. Clin. Immunol. 20: 10-16, 2000).

While the etiologies of the autoimmune diseases and experimental models of autoimmune diseases do have different etiologies, the prior art, as well as applicant's disclosure recognized that the ordinary artisan could target inflammatory mediators (e.g. cells) associated with these conditions in order to treat these conditions with an expectation of success at the time the invention was made. Again, it is noted that Wayner et al. does teach targeting a number of inflammatory or autoimmune conditions, including rheumatoid arthritis. In addition, given that the teachings of Bendig et al. to treat the highly difficult case of multiple sclerosis, the ordinary artisan would have had a reasonable expectation of success in treating other autoimmune conditions such as rheumatoid arthritis.

Also, it is noted that Example 9 of the instant specification discloses the efficacy of the humanized 21.6 antibody in the prophylactic and therapeutic treatment of EAE in an animal model simulating multiple sclerosis in humans. Therefore, applicant has relied upon experimental models of treating EAE to support the ability of the humanized 21.6 antibody to treat autoimmune diseases encompassing rheumatoid arthritis as well as multiple sclerosis (also, see Section VII, Methods of Treatment on pages 25-31 of the instant specification).

In addition, the Background of the Invention of the instant specification is consistent with the prior art that $\alpha 4$ is a therapeutic target to treat pathologic inflammation by inhibiting over-responsive leukocytes. It is noted that Wayner et al. discloses a number of diseases including autoimmune diseases such as rheumatoid arthritis and multiple sclerosis with a common mode of action to Bendig et al. as well as the instant application.

Applicant has not addressed the clear teachings of the prior art drawn to inhibiting deleterious inflammation by targeting leukocytes with $\alpha 4$ -specific antibodies to treat a number of inflammatory and autoimmune conditions, which is consistent with the same mode of action relied upon by the instant disclosure.

In response to applicant's arguments that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See In re Fine 5 USPQ2d 1596 (Fed. Cir 1988) and In re Jones 21 USPQ2d 1941 (Fed. Cir. 1992). In this case the teachings of both Wayner et al. and Bendig et al. teach inhibiting the inflammatory responses in autoimmune responses with $\alpha 4$-specific antibodies, including rheumatoid arthritis and the particular humanized 21.6 antibody of the claimed invention and the teachings of both Wayner et al. and Bendig et al. teach and claim success in treating inflammatory conditions to solve the same or nearly the same problems of pathologic inflammation in inflammatory and autoimmune conditions by targeting leukocytes with $\alpha 4$-specific antibodies would have led one of ordinary skill in the art at the time the invention was made to combine the references to solve a well known problem in the art.

The strongest rationale for combining reference is a recognition, expressly or implicitly in the prior art or drawn from a convincing line of reasoning based on established scientific principles or legal precedent that some advantage or expected beneficial result would have been produced by their combination In re Sernaker 17 USPQ 1, 5-6 (Fed. Cir. 1983) see MPEP 2144

Applicant's arguments are not found persuasive.

9. Upon reconsideration of applicant's amended claims and arguments in conjunction with The Yednock declaration under 37 C.F.R. § 1.132, filed 10/24/02 (Paper Nos. 19/20), the previous rejection under 35 U.S.C. § 103(a) as being unpatentable over Wayner et al. (U.S. Patent No. 5,730,978) in view of Monshizadegan et al. (Agents Actions 39: C177-179, 1993; IDS, #25) OR Yednock et al. (U.S. Patent No. 6,033,665) and further in view of known methods to humanized antibodies of interest for human therapy as taught by Queen et al. (U.S. Patent No. 5,530,101; IDS, #2), Bendig et al. (WO 92/15683) and Kettleborough et al. (Protein Engineering 4: 773-783, 1991; IDS, #23) has been withdrawn.

10. No claim is allowed.

11. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL.** See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
January 6, 2003